

### REMARKS

Upon entry of this third preliminary amendment, claims 45-88 are in this application. These claims correspond to those entered via Article 34 amendments in the corresponding International application. New claims 45-88 are supported throughout the specification. A copy of the pending claims is attached as Appendix A. No new matter is added by this preliminary amendment.

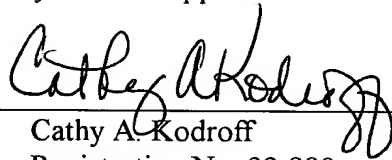
Applicants respectfully request consideration of the pending claims.

The Director of the U. S. Patent and Trademark Office is hereby authorized to charge any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees to our Deposit Account No. 08-3040.

Respectfully submitted,

HOWSON AND HOWSON  
Attorneys for the Applicants

By



Cathy A. Kodroff  
Registration No. 33,980  
Spring House Corporate Center  
Box 457  
Spring House, PA 19477  
Telephone: (215) 540-9210  
Telefacsimile: (215) 540-5818



## APPENDIX A - PENDING CLAIMS

45. A method for reducing or eliminating the susceptibility of a tropoelastin to proteolysis comprising mutating a sub-sequence in the tropoelastin so that the susceptibility of the tropoelastin to proteolysis is reduced or eliminated.
46. A method according to claim 45 wherein one sub-sequence is mutated.
47. A method according to claim 45 wherein one amino acid residue in the sub-sequence is mutated.
48. A method according to claim 45 wherein the sub-sequence is capable of being digested by a serine protease.
49. A method according to claim 48 wherein the sub-sequence has an amino acid sequence including the sequence: RAAAG.
50. A method according to claim 49 wherein the sub-sequence is mutated by replacing arginine in the sequence: RAAAG with alanine.
51. A method according to claim 48 wherein the sub-sequence has an amino acid sequence selected from the group of sequences shown in SEQ ID NOS: 17 to 44.
52. A method according to claim 51 wherein the sub-sequence is mutated by replacing arginine in the sequence selected from the group of sequences shown in SEQ ID NOS: 17 to 44 with alanine.

53. A method according to claim 48 wherein the sub-sequence is capable of being digested by thrombin and has an amino acid sequence shown in SEQ ID NOS: 8 or 9.

54. A method according to claim 48 wherein the sub-sequence is capable of being digested by plasmin and has an amino acid sequence shown in SEQ ID NOS: 11 or 12.

55. A method according to claim 48 wherein the sub-sequence is capable of being digested by kallikrein.

56. A method according to claim 55 wherein the sub-sequence has an amino acid sequence shown in SEQ ID NOS: 9 or 10.

57. A method according to claim 45 wherein the sub-sequence is capable of being digested by a metalloproteinase.

58. A method according to claim 57 wherein the sub-sequence has an amino acid sequence including the sequence: ALAAA.

59. A method according to claim 58 wherein the sub-sequence is mutated by replacing alanine at any position in the sequence: ALAAA with another amino acid residue.

60. A method according to claim 59 wherein the sub-sequence is mutated by replacing the alanine which is N-terminal to leucine in the sequence: ALAAA with another amino acid.

61. A method according to claim 57 wherein the sub-sequence has an amino acid sequence selected from the group of sequences shown in SEQ ID NOS: 45 to 70.

62. A method according to claim 61 wherein the sub-sequence is mutated by replacing alanine at any position in the sequence selected from the group of sequences shown in SEQ ID NOS: 45 to 70 with another amino acid residue.

63. A method according to claim 62 wherein the alanine that is replaced is N-terminal to leucine.

64. A method according to claim 57 wherein the sub-sequence is capable of being digested by gelatinase A or B.

65. A method according to claim 64 wherein the sub-sequence has an amino acid sequence shown in SEQ ID NO: 13.

66. A method according to any one of claims 45 to 65 wherein the tropoelastin is human tropoelastin.

67. A method for enhancing the susceptibility of a tropoelastin to proteolysis comprising inserting a sub-sequence into the tropoelastin so that the susceptibility of the tropoelastin to proteolysis is enhanced.

68. A method according to claim 67 wherein one sub-sequence is inserted.

69. A method according to claim 67 wherein the inserted sub-sequence is capable of being digested with a serine protease.

70. A method according to claim 69 wherein the inserted sub-sequence has an amino acid sequence including the sequence: RAAAG.

71. A method according to claim 69 wherein the inserted sub-sequence has an amino acid sequence selected from the group of sequences shown in SEQ ID NOS: 17 to 44.

72. A method according to claim 69 wherein the inserted sub-sequence is capable of being digested by thrombin and has an amino acid sequence shown in SEQ ID NOS: 8 or 9.

73. A method according to claim 69 wherein the inserted sub-sequence is capable of being digested by plasmin and has an amino acid sequence shown in SEQ ID NOS: 11 or 12.

74. A method according to claim 69 wherein the inserted sub-sequence is capable of being digested by kallikrein.

75. A method according to claim 74 wherein the inserted sub-sequence has an amino acid sequence shown in SEQ ID NOS: 9 or 10.

76. A method according to claim 67 wherein the inserted sub-sequence is capable of being digested by a metalloproteinase.

77. A method according to claim 76 wherein the inserted sub-sequence has an amino acid sequence including the sequence: ALAAA.

78. A method according to claim 76 wherein the inserted sub-sequence has an amino acid sequence selected from the group of sequences shown in SEQ ID NOS: 45 to 70.

79. A method according to claim 76 wherein the inserted sub-sequence is capable of being digested by gelatinase A or B.

80. A method according to claim 79 wherein the inserted sub-sequence has the amino acid sequence shown in SEQ ID NO: 13.

81. A method according to any one of claims 67 to 80 wherein the tropoelastin is human tropoelastin.

82. A peptidomimetic molecule comprising all or part of a peptide selected from the group consisting of KAPGVGGAF, RAAAGLG, RSLSPELREGD, KAAQFGLVPGV, KSAAKVAAKAQLRAA, RSLSPELRE AND LAAAKAAKYGAA.

83. A peptidomimetic molecule which has the sequence: H-Ala-Ala-Lys-Ala-Gln-Leu-Arg-Ala-Ala-Ala-Gly-Leu-Gly-Ala-OH or H-Ala-Ala-Lys-Ala-Gln-Leu-Arg-R-Ala-Ala-Ala-Gly-Leu-Gly-Ala-OH (where R = a reduced peptide bond).

84. A peptidomimetic molecule which is a retro-inverso pseudo peptide which has the sequence: H-D-Ala-Gly-D-Leu-Gly-D-Ala-D-Ala-D-Ala-(R)-D-Arg-D-Leu-D-Gln-D-Ala-D-Lys-D-Ala-D-Ala-OH (where R = a reduced peptide bond) or H-D-Ala-Gly-D-Leu-Gly-D-Ala-D-Ala-D-Ala-D-Arg-D-Leu-D-Gln-D-Ala-D-Lys-D-Ala-D-Ala-OH.

85. A peptidomimetic molecule which has the sequence H-Val-Pro-Gly-Ala-Leu-Ala-Ala-Ala-OH or H-Val-Pro-Gly-Ala-(R)-Leu-Ala-Ala-Ala-OH (where R = a reduced peptide bond).

86. A peptidomimetic molecule which is a retro-inverso pseudo peptide which has the sequence: H-D-Ala-D-Ala-D-Ala-D-Leu-(R)-D-Ala-Gly-D-Pro-D-Val-OH (where R = a reduced peptide bond) or H-D-Ala-D-Ala-D-Ala-D-Leu-D-Ala-Gly-D-Pro-D-Val-OH.

87. A method for enhancing the purification of a tropoelastin comprising including a peptidomimetic molecule according to any one of claims 82 to 86 in a crude tropoelastin preparation which is being subjected to purification.

88. A pharmaceutical composition comprising a peptidomimetic molecule according to any one of claims 82 to 86 and a pharmaceutically acceptable carrier.